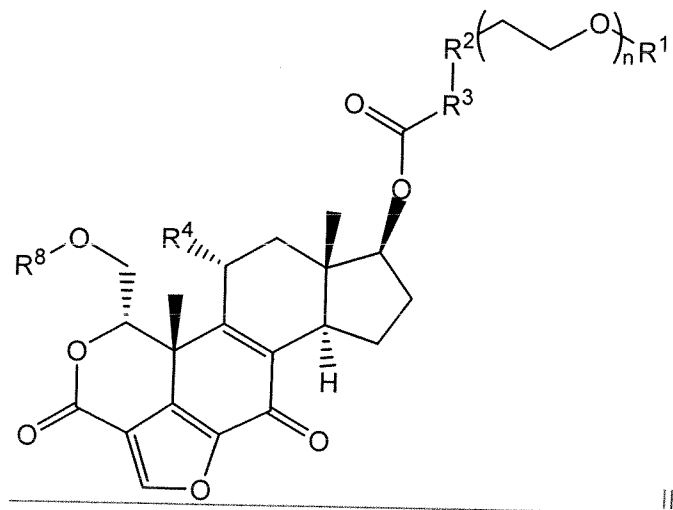
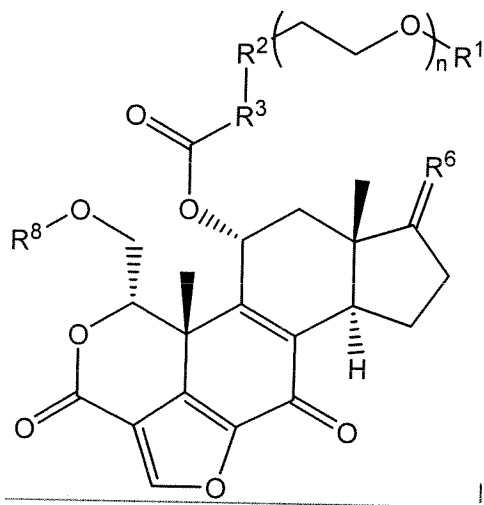
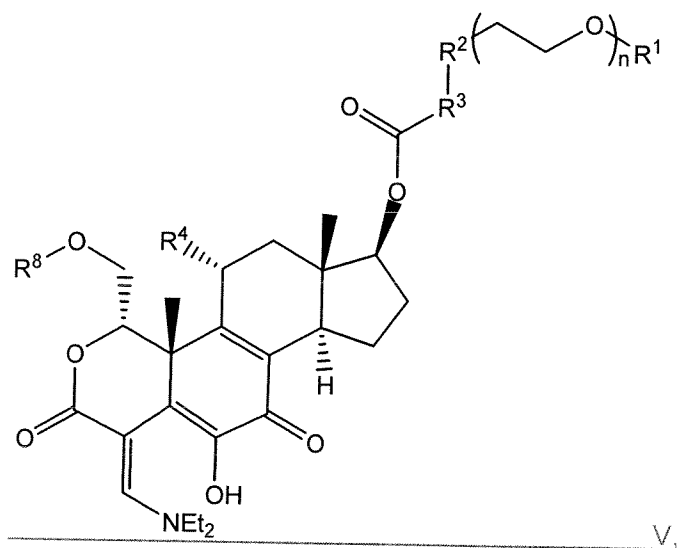
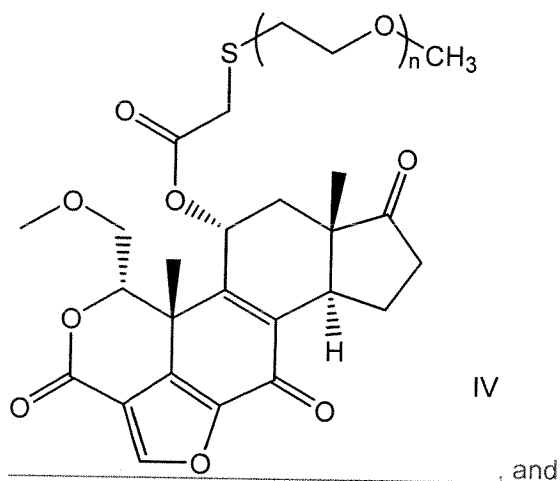
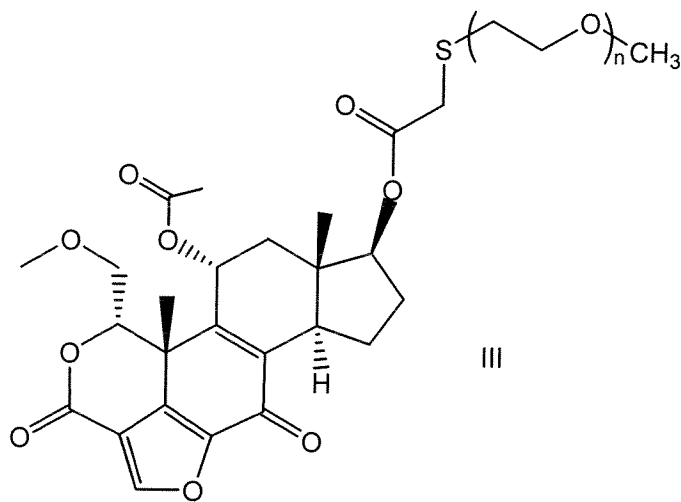


LISTING OF CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in this application.

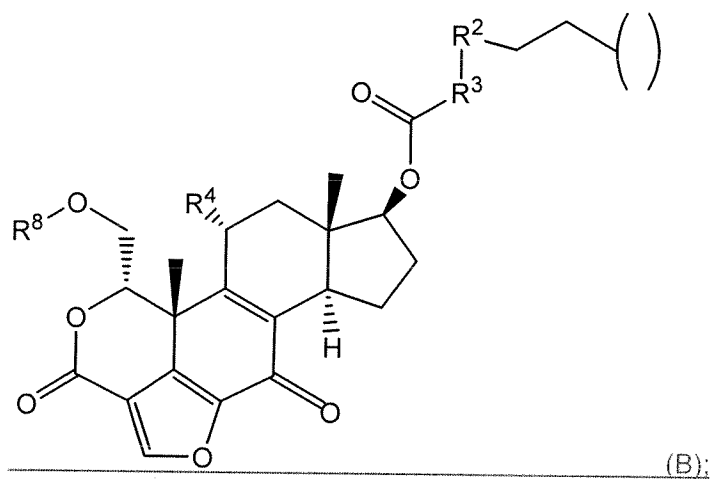
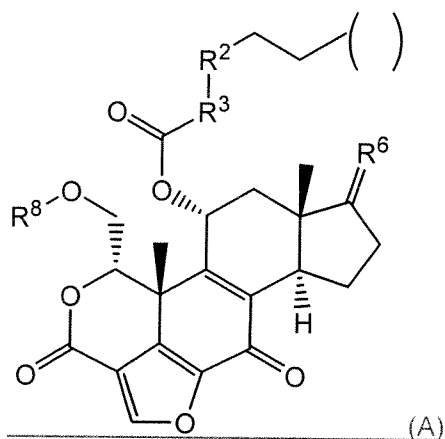
1. (Currently Amended) A water-soluble drug-polymer conjugate selected from a conjugate of formula I, II, III, IV and V:





wherein

R^1 is alkyl, a drug-polymer conjugate of formula (A) or a drug-polymer conjugate of formula (B):



R^2 is -O-, -NH-, or -S-;

R^3 is alkyl, a cycloalkyl, or aryl;

R^4 is H, =O, -O-COC₄H₉, or OR⁷;

R^6 is =O or OR⁷;

R^7 is H, COR⁹ or alkyl;

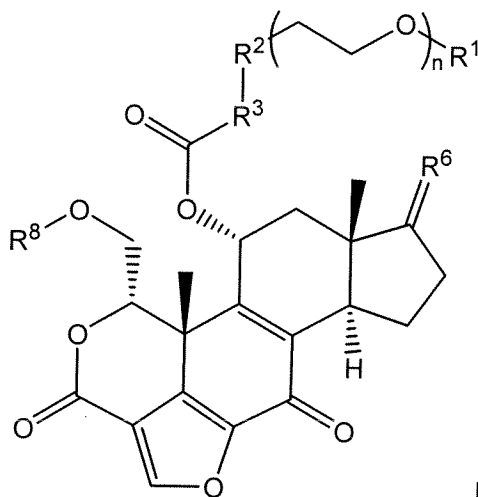
R^8 is alkyl or H;

R^9 is alkyl, H, aryl, or -CH₂Ar; and

~~n is 1-1000 having the general formula P-X-D: wherein, P is a water-soluble polymer; D is a wortmannin derivative; and X is a covalent linkage between a water-soluble polymer and the wortmannin derivative.~~

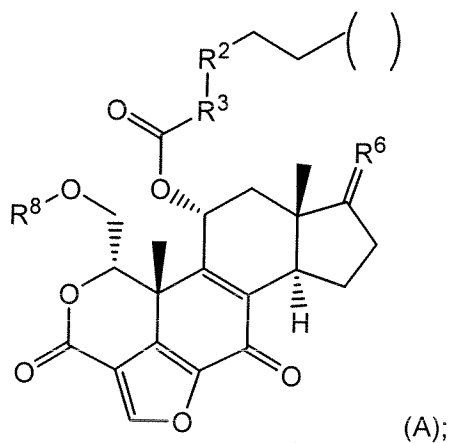
2. (Original) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 1 and a pharmaceutically acceptable carrier.
3. (Original) A method for treating or inhibiting a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 1.
4. (Original) A method of claim 3 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.
5. (Original) A method of claim 3 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.
6. (Original) A method of claim 3 wherein treating or inhibiting comprises inhibition of PI3 kinase.
7. (Original) A method of claim 3 wherein treating or inhibiting comprises inhibition of TOR kinase.
8. (Original) A method of claim 3 wherein the pathological condition is non-small cell lung cancer.
9. (Withdrawn) A method of claim 3 wherein the pathological condition is brain cancer, ischaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.
10. (Withdrawn) A method of claim 3 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.
11. (Withdrawn) A method of claim 10 wherein the agent is interferon- α .

12. (Withdrawn) A method of claim 10 wherein the agent is pegylated rapamycin.
13. (Withdrawn) A method of claim 10 wherein the agent is a cytotoxic.
14. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula I



wherein:

R^1 is alkyl, or a drug-polymer conjugate of formula (A)



R^2 is -O-, -NH-, or -S-;

R^3 is alkyl, a cycloalkyl, or aryl;

R^6 is =O or OR^7 ;

R^7 is H, COR^9 or alkyl;

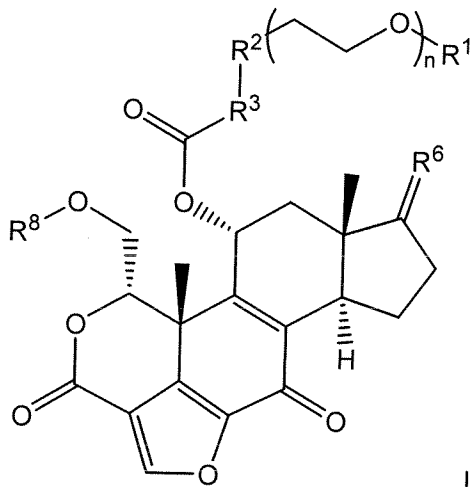
R⁸ is alkyl or H;

R⁹ is alkyl, H, aryl, or -CH₂Ar; and

n is 1-1000.

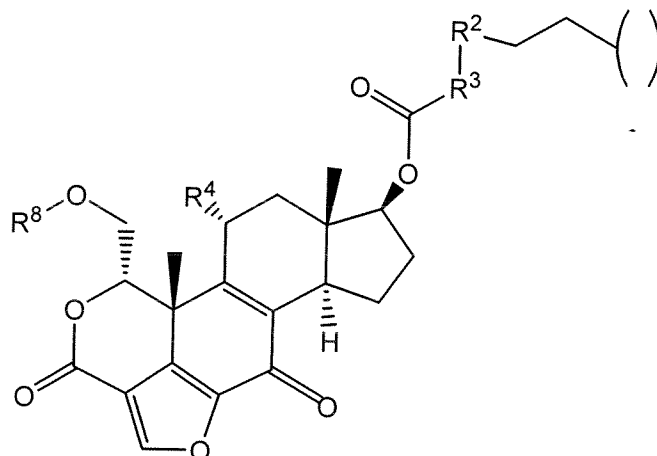
15. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein n is 250 – 400.
16. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein n is 50 – 150.
17. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein the molecular weight of polymer is from about 400 to about 80,000.
18. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein the molecular weight of polymer from about 1000 to about 8000.
19. (Withdrawn) The water-soluble drug-polymer conjugate of claim 14 wherein the molecular weight of polymer is from about 4000 to about 6000.
20. (Withdrawn) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 14 and a pharmaceutically acceptable carrier.
21. (Withdrawn) A method for treating or inhibiting a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 14.
22. (Withdrawn) A method of claim 21 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.
23. (Withdrawn) A method of claim 21 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.
24. (Withdrawn) A method of claim 21 wherein treating or inhibiting comprises inhibition of PI3 kinase.
25. (Withdrawn) A method of claim 21 wherein treating or inhibiting comprises inhibition of TOR kinase.

26. (Withdrawn) A method of claim 21 wherein the pathological condition is non-small cell lung cancer.
27. (Withdrawn) A method of claim 21 wherein the pathological condition is brain cancer, ischaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.
28. (Withdrawn) A method of claim 21 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.
29. (Withdrawn) A method of claim 28 wherein the agent is interferon- α .
30. (Withdrawn) A method of claim 28 wherein the agent is pegylated rapamycin.
31. (Withdrawn) A method of claim 28 wherein the agent is a cytotoxic.
32. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula I:



wherein:

R^1 is alkyl, or a drug-polymer conjugate of formula (B)



(B);

R^2 is -O-, -NH-, or -S-;

R^3 is alkyl, a cycloalkyl, or aryl;

R^4 is H, =O, -O-COC₄H₉, or OR⁷;

R^7 is H, COR⁹ or alkyl;

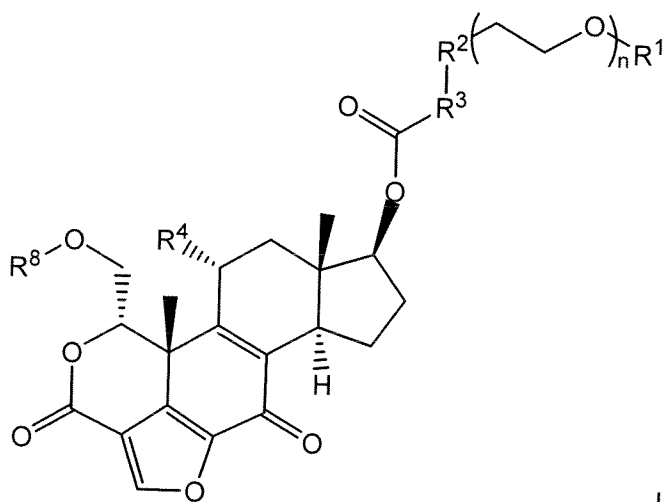
R^8 is alkyl or H;

R^9 is alkyl, H, aryl, or -CH₂Ar; and

n is 1-1000.

33. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein n is 250 – 400.
34. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein n is 50 – 150.
35. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein the molecular weight of polymer is from about 400 to about 80,000.
36. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein the molecular weight of polymer is from about 1000 to about 8000.
37. (Withdrawn) The water-soluble drug-polymer conjugate of claim 32 wherein the molecular weight of polymer is from about 4000 to about 6000.

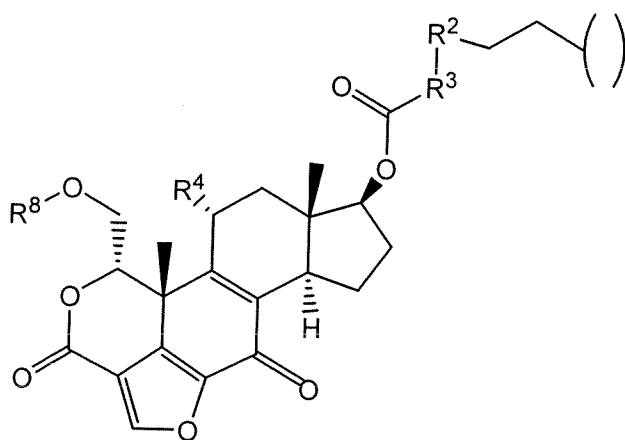
38. (Withdrawn) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 32 and a pharmaceutically acceptable carrier.
39. (Withdrawn) A method for treating or inhibiting a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 32.
40. (Withdrawn) A method of claim 39 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.
41. (Withdrawn) A method of claim 39 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.
42. (Withdrawn) A method of claim 39 wherein treating or inhibiting comprises inhibition of PI3 kinase.
43. (Withdrawn) A method of claim 39 wherein treating or inhibiting comprises inhibition of TOR kinase.
44. (Withdrawn) A method of claim 39 wherein the pathological condition is non-small cell lung cancer.
45. (Withdrawn) A method of claim 39 wherein the pathological condition is brain cancer, ischaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.
46. (Withdrawn) A method of claim 39 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.
47. (Withdrawn) A method of claim 46 wherein the agent is interferon- α .
48. (Withdrawn) A method of claim 46 wherein the agent is pegylated rapamycin.
49. (Withdrawn) A method of claim 46 wherein the agent is a cytotoxic.
50. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula II



II

wherein:

R^1 is alkyl, or a drug-polymer conjugate of formula (B)



(B);

R^2 is -O-, -NH-, or -S-;

R^3 is alkyl, a cycloalkyl, or aryl;

R^4 is H, =O, -O-COC₄H₉, or OR⁷;

R^7 is H, COR⁹ or alkyl;

R^8 is alkyl or H;

R^9 is alkyl, H, aryl, or -CH₂Ar; and

n is 1-1000.

51. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein n is 250 – 400.
52. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein n is 50 – 150.
53. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein the molecular weight of polymer is from about 400 to about 80,000.
54. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein the molecular weight of polymer is from about 1000 to about 8000.
55. (Withdrawn) The water-soluble drug-polymer conjugate of claim 50 wherein the molecular weight of polymer is from about 4000 to about 6000.
56. (Withdrawn) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 50 and a pharmaceutically acceptable carrier.
57. (Withdrawn) A method for treating or inhibiting a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 50.
58. (Withdrawn) A method of claim 57 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.
59. (Withdrawn) A method of claim 57 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.
60. (Withdrawn) A method of claim 57 wherein treating or inhibiting comprises inhibition of PI3 kinase.
61. (Withdrawn) A method of claim 57 wherein treating or inhibiting comprises inhibition of TOR kinase.
62. (Withdrawn) A method of claim 57 wherein the pathological condition is non-small cell lung cancer.
63. (Withdrawn) A method of claim 57 wherein the pathological condition is brain cancer, ischaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.

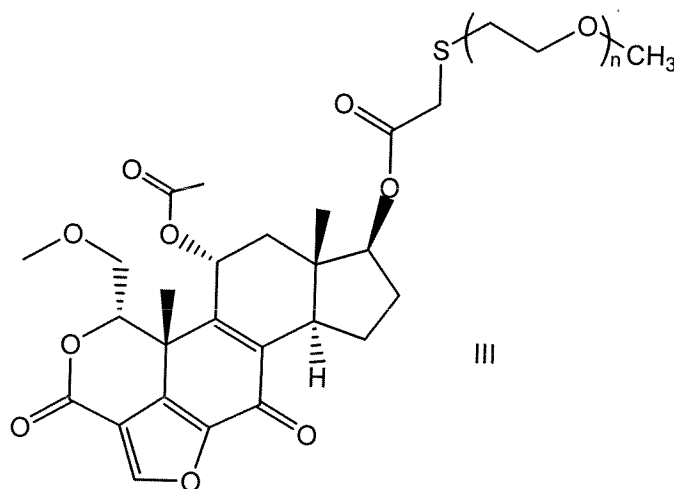
64. (Withdrawn) A method of claim 57 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.

65. (Withdrawn) A method of claim 64 wherein the agent is interferon- α .

66. (Withdrawn) A method of claim 64 wherein the agent is pegylated rapamycin.

67. (Withdrawn) A method of claim 64 wherein the agent is a cytotoxic.

68. (Original) A water-soluble drug-polymer conjugate having the structure of formula III:



n is 1-1000.

69. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein n is 250-400.

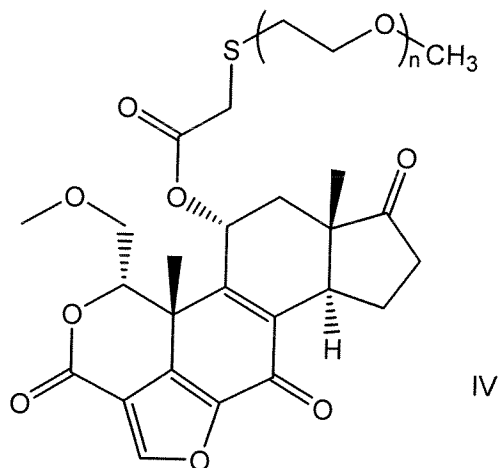
70. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein n is 50-150.

71. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein the molecular weight of polymer is from about 400 to about 80,000.

72. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein the molecular weight of polymer is from about 1000 to about 8000.

73. (Original) The water-soluble drug-polymer conjugate of claim 68 wherein the molecular weight of polymer is from about 4000 to about 6000.

74. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula IV:



wherein $n = 1-1000$.

75. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein n is 250 – 400.

76. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein n is 50 – 150.

77. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein the molecular weight of polymer is from about 400 to about 80,000.

78. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein the molecular weight of polymer is from about 1000 to about 8000.

79. (Withdrawn) The water-soluble drug-polymer conjugate of claim 74 wherein the molecular weight of polymer is from about 4000 to about 6000.

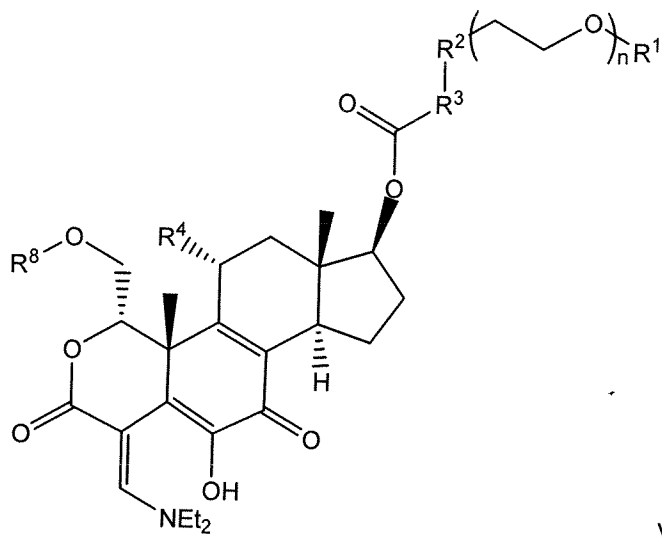
80. (Withdrawn) A pharmaceutical composition comprising the water-soluble drug-polymer conjugate of claim 74 and a pharmaceutically acceptable carrier.

81. (Withdrawn) A method for treating or inhibiting a pathological condition or disorder mediated in a mammal comprising providing to said mammal an effective amount of a water-soluble drug-polymer conjugate of claim 74.

82. (Withdrawn) A method of claim 81 wherein the effective amount of the water-soluble drug-polymer is 10 to 1000 mg/kg.
83. (Withdrawn) A method of claim 81 wherein the effective amount of the water-soluble drug-polymer is 0.5 to 10 mg/kg.
84. (Withdrawn) A method of claim 81 wherein treating or inhibiting comprises inhibition of PI3 kinase.
85. (Withdrawn) A method of claim 81 wherein treating or inhibiting comprises inhibition of TOR kinase.
86. (Withdrawn) A method of claim 81 wherein the pathological condition is non-small cell lung cancer.
87. (Withdrawn) A method of claim 81 wherein the pathological condition is brain cancer, ischaemic heart disease, restenosis, inflammation, platelet aggregation, sclerosis, respiratory disorder, HIV and bone resorption.
88. (Withdrawn) A method of claim 81 wherein providing an effective amount is alone or in combination with other agents that modulate growth factor signaling, cytokine response, and cell cycle control.
89. (Withdrawn) A method of claim 88 wherein the agent is interferon- α .
90. (Withdrawn) A method of claim 88 wherein the agent is pegylated rapamycin.
91. (Withdrawn) A method of claim 88 wherein the agent is a cytotoxic.
92. (Withdrawn) A process for the preparation of a water-soluble drug-polymer conjugate of claim 68 comprising:
- a. adding a solvent to 17-dihydro-17-(1-iodoacetyl)-wortmannin to obtain a solution;
 - b. adding a tertiary amine or sodium bicarbonate to the solution;
 - c. adding mPEG-sulfhydryl 5000 to the solution of step (b);
 - d. stirring the solution of step (c) for 30 minutes;
 - e. adding ether to the stirred solution;
 - f. collecting the solid; and

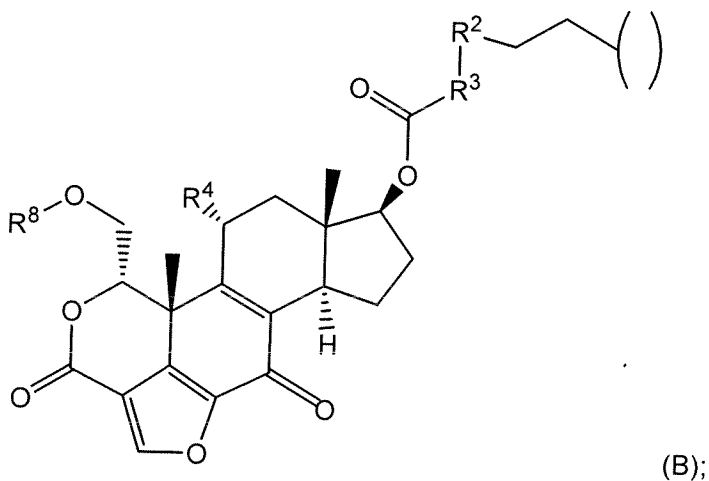
- g. washing the collected solid with ether to obtain the pegylated wortmannin derivative.

93. (Withdrawn) A water-soluble drug-polymer conjugate having the structure of formula V:



wherein:

R¹ is alkyl, or a drug-polymer conjugate of a single non-repeating formula (V)



R² is -O-, -NH-, or -S-;

R³ is alkyl, a cycloalkyl, or aryl;

R⁴ is H, =O, -O-COC₄H₉, or OR⁷;

R⁷ is H, COR⁹ or alkyl;

R⁸ is alkyl or H;

R⁹ is alkyl, H, aryl, or -CH₂Ar; and

n is 1-1000.

94. (Withdrawn) A process for the preparation of the compound of claim 93 comprising addition of an amine to a compound of claim 50 to obtain a compound of claim 93.

95. (Withdrawn) A process of claim 94 wherein the amine comprises diethyl amine.

96. A process for the preparation of a water-soluble drug-polymer conjugate of claim 74 comprising:

- a) adding a solvent to 11-desacetyl-11-(1-iodoacetyl)-wortmannin to obtain a solution;
- b) adding a tertiary amine to the solution;
- c) adding mPEG-sulfhydryl 5000 to the solution of step (b);
- d) stirring the solution of step (c) for 30 minutes;
- e) adding ether to the stirred solution;
- f) collecting the solid; and
- g) washing the collected solid with ether to obtain the pegylated wortmannin derivative, as disclosed.